III JORNADA TRASLACIONAL
DE ONCOLOGÍA DE PRECISIÓN:
A TRAVÉS DE LAS VÍAS DE SEÑALIZACIÓN
SEVILLA, 12 Y 13 DE FEBRERO DE 2026

AntiTROP2 en Cáncer de mama Luminal

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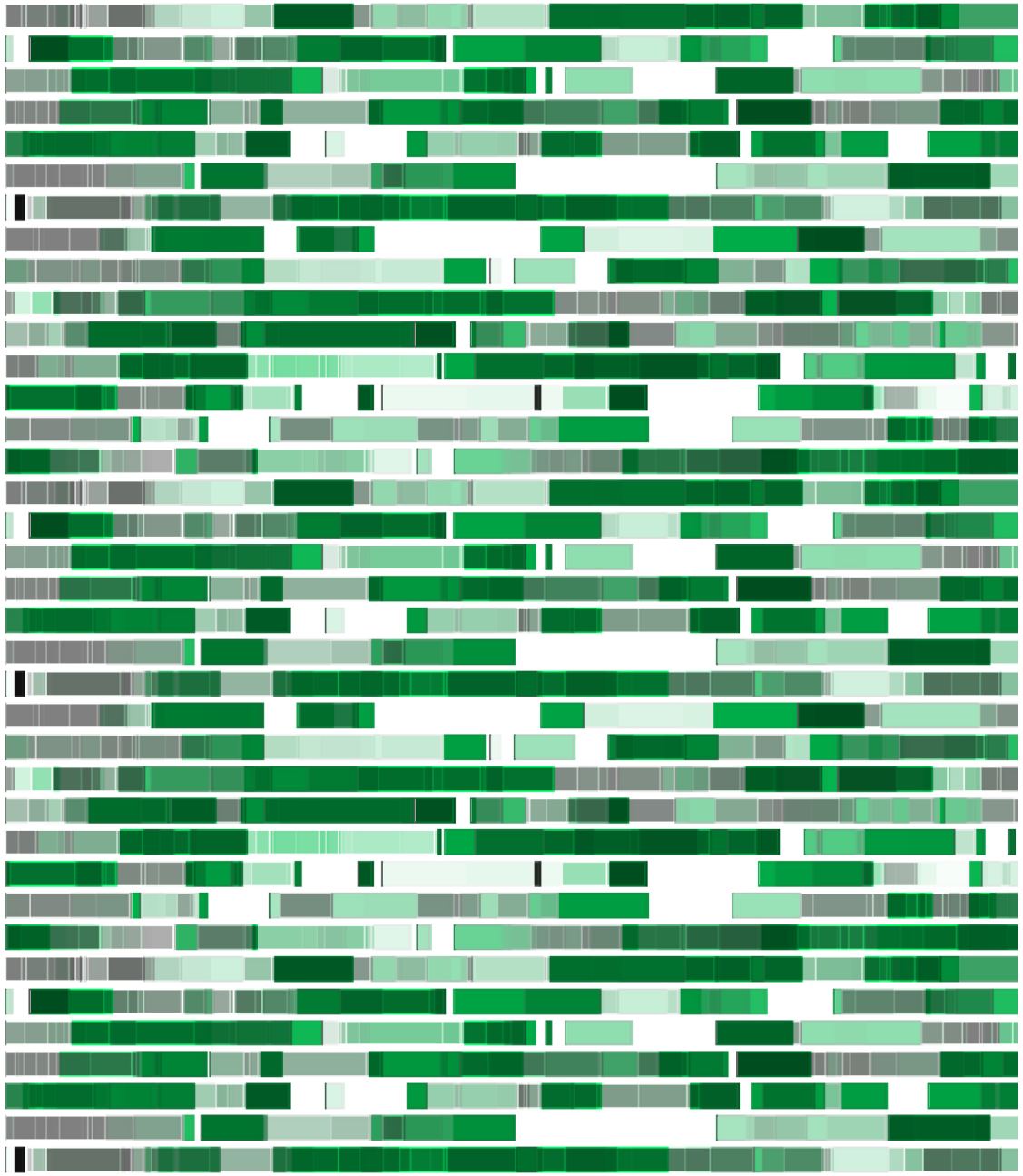
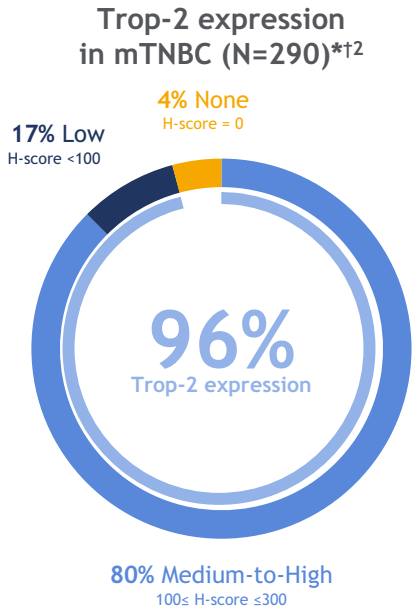


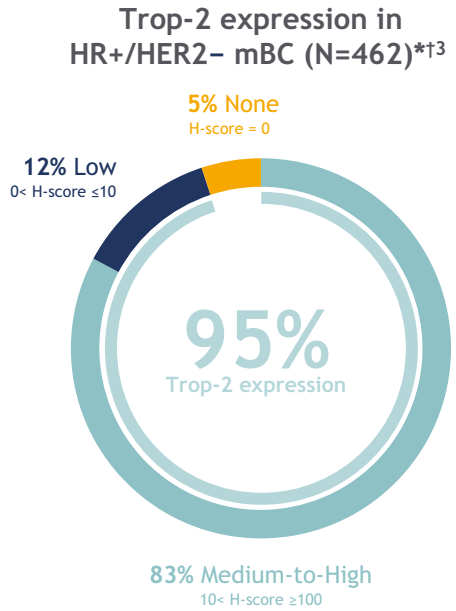
Organizador por:
HENDERE HEALTHCARE

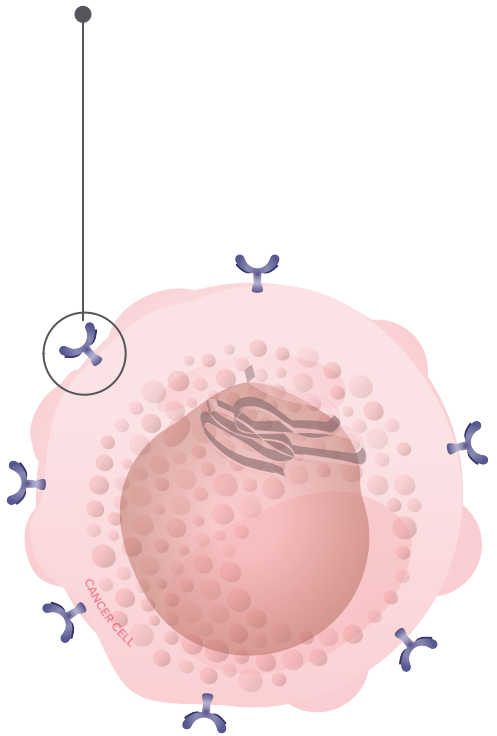
Introducción

Trop-2 está altamente expresado en cáncer de mama HR+ HER2- metastásico

Trop-2 is a transmembrane glycoprotein expressed in various epithelial cancers as a tumour-associated calcium signal transducer that is functionally linked to cell migration and anchorage-independent growth[1]

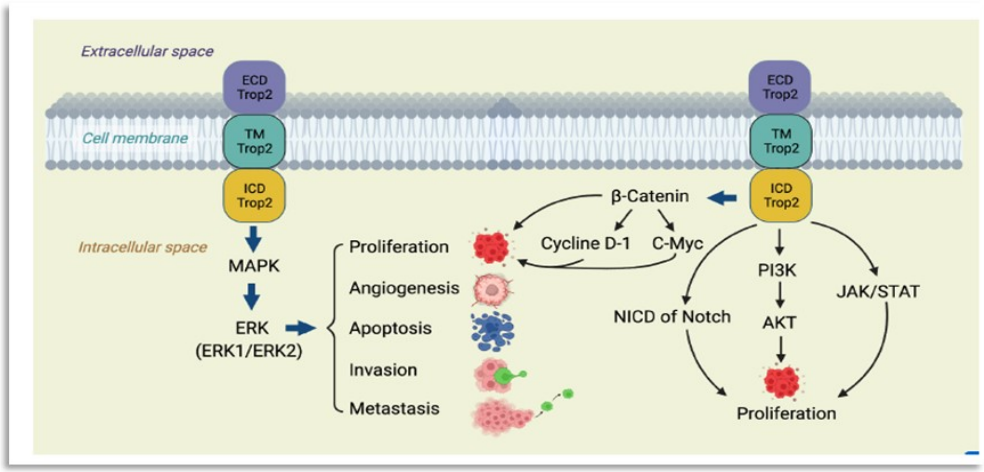


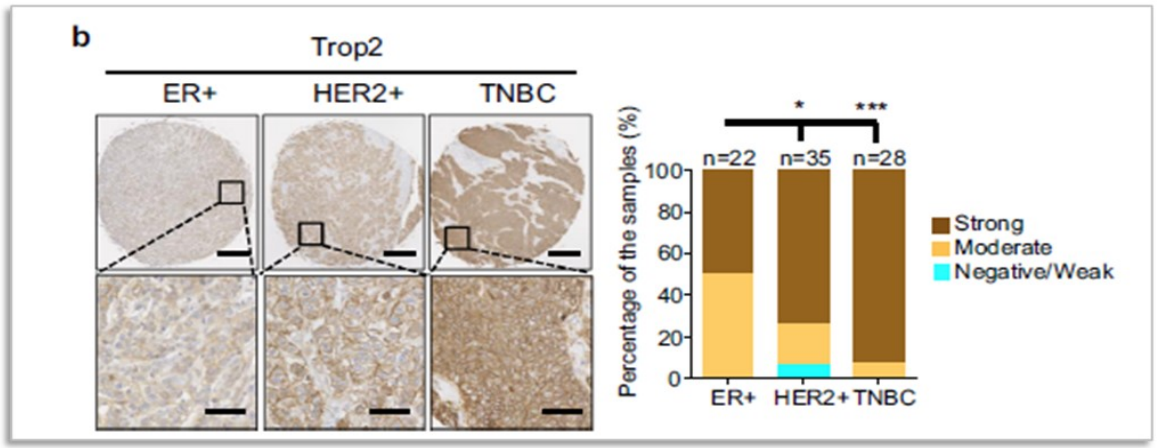




Adapted from: 1. Goldenberg DM, et al. *Oncotarget*. 2015;6:22496-22512; 2. Bardia A, et al. *Ann Oncol*. 2021;32:1148-1156; 3. Rugo HS, et al. Presented at SABCS Annual Meeting 2022. 6-10 December. San Antonio, TX. Abstract #GS1-11

Why ADCs targeting TROP2 in HR+/HER2- ABC?



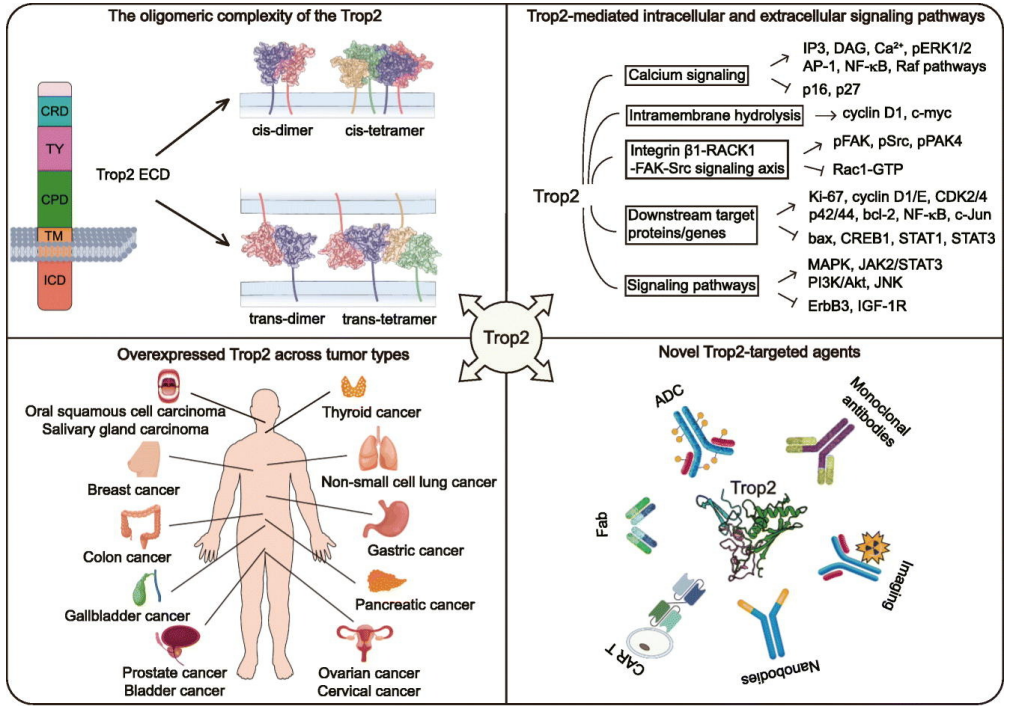


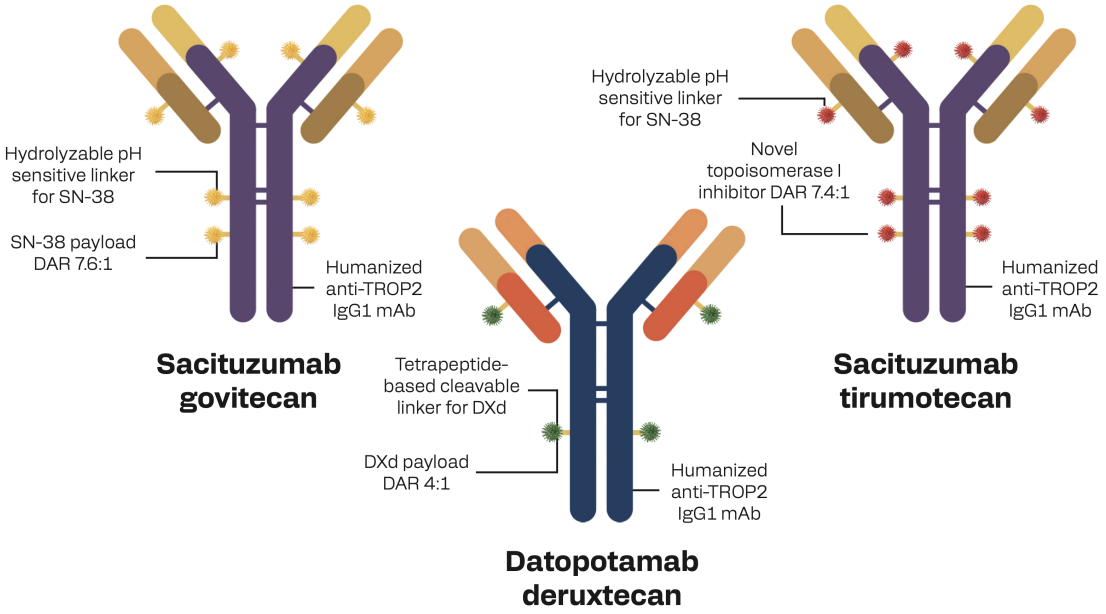
Cancer cell proliferation, invasion, survival
Associated with EMT (some cancer types)

TROP-2 is overexpressed in 50-60% of HR+ BC

Shvartsur et al, Genes & Cancer 2015; Rugo. SABCS 2022. Abs GS1-11; Tolaney S et al, ASCO 2023 Abs 1003; ; Bardia et al, Ann Oncol 2021; Zhao et al, Oncol Rep 2018 ; Yao et al, Front Oncol 2023; Aslan et al, NPJ Breast Cancer 2021

ADCs AntiTROP2



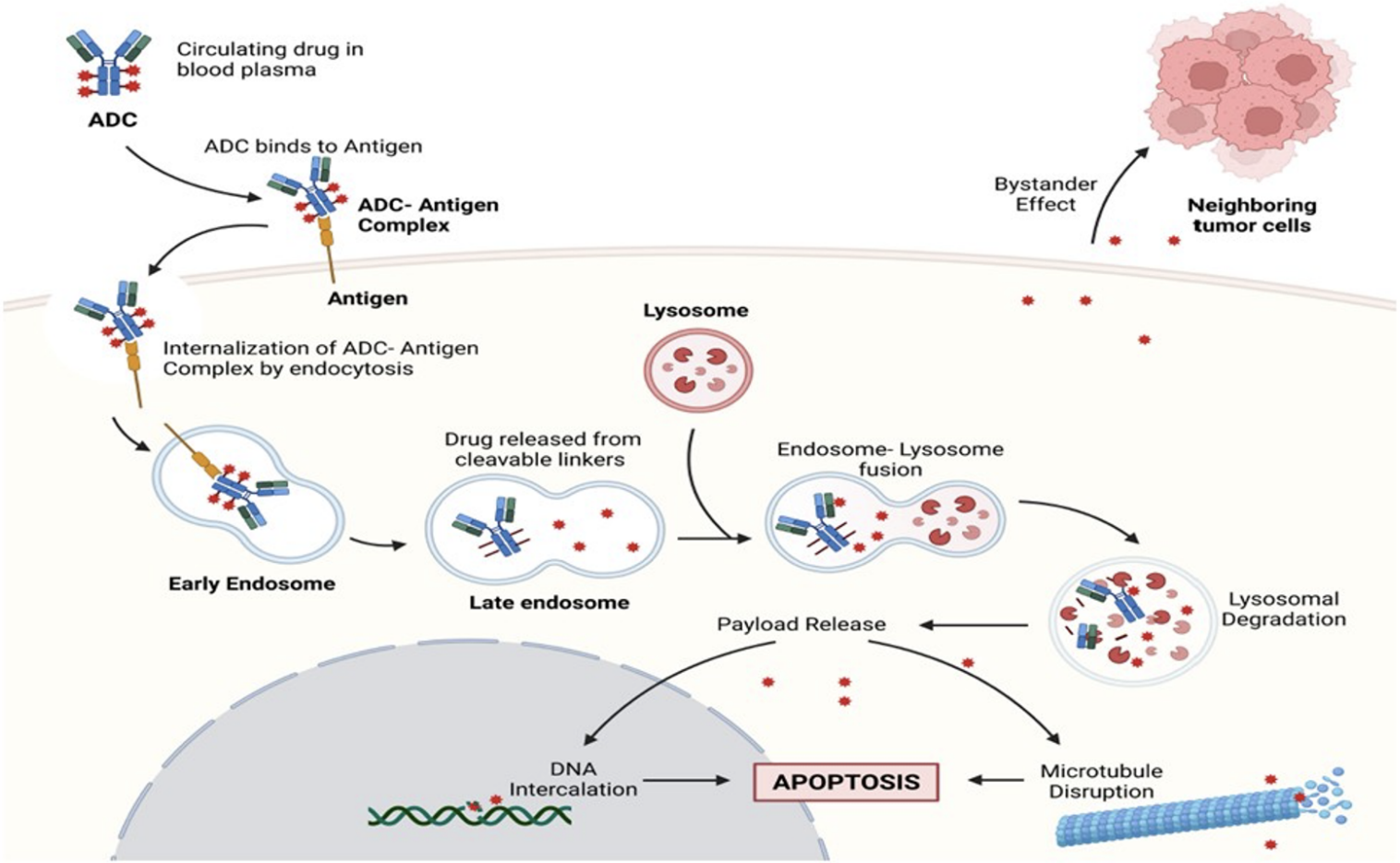


Trop2 es un antigeno de superficie celular sobreexpresado en más del 95% de los tumores HR+ y baja expresión en la mayoría de tejidos normales.

Todos los ADCs utilizan inhibidores de la Topoisomerasa I que promueve roturas de cadena DNA y consigue que la célula tumoral entre en senescencia y apoptosis.

http://www.cancernetwork.com/view/3-things-you-should-know-about-trop2-as-a-therapeutic-target-in-triple-negative-breast-cancer *Liu et al Pharmacol Ther 2022*

Mecanismo de acción ADCs



Larose et al. Cancer Drug Resist. 2025.

Evidencia

TROPICS-02 Estudio Fase 3 Sacituzumab Govitecan en CMM Luminal

Metastatic or locally recurrent inoperable HR+/HER2− breast cancer that progressed after[a]

- At least 1 endocrine therapy, taxane, and CDK4/6 inhibitor in any setting
- At least 2, but no more than 4, lines of chemotherapy for metastatic disease
- Measurable disease by RECIST 1.1

N=543

R 1:1

Treatment was continued until progression or unacceptable toxicity

Sacituzumab govitecan
10 mg/kg IV
days 1 and 8, every 21 days
n=272

Treatment of physician's choice[b]
(capecitabine, vinorelbine, gemcitabine or eribulin)
n=271

Endpoints

Primary
- PFS by BICR

Secondary
- OS
- ORR, DOR, CBR by LIR and BICR
- PRO
- Safety

Stratification:
- Visceral metastases (yes/no)
- Endocrine therapy in metastatic setting ≥6 months (yes/no)
- Prior lines of chemotherapies (2 vs 3/4)

Hugo, Lancet 2023

Población

	SG (n=272)	TPC (n=271)
Female, n (%)	270 (99)	268 (99)
Median age, y (range)	57 (29-86)	55 (27-78)
<65 y, n (%)	199 (73)	204 (75)
≥65 y, n (%)	73 (27)	67 (25)
Race or ethnic group, n (%)		
White	184 (68)	178 (66)
Black	8 (3)	13 (5)
Asian	11 (4)	5 (2)
Other[a] / Not reported[b]	69 (25)	75 (28)
ECOG PS, n (%)		
0	116 (43)	126 (46)
1	156 (57)	145 (54)
Visceral metastases at baseline, n (%)	259 (95)	258 (95)
Liver metastases,[c] n (%)	229 (84)	237 (87)
De novo metastatic breast cancer, n (%)	78 (29)	60 (22)

	SG (n=272)	TPC (n=271)
Median time from initial metastatic diagnosis to randomization, mo (range)	48.5 (1.2- 243.8)	46.6 (3.0- 248.8)
Prior chemotherapy in (neo)adjuvant setting, n (%)	173 (64)	184 (68)
Prior endocrine therapy use in the metastatic setting ≥6 mo, n (%)	235 (86)	234 (86)
Prior CDK4/6 inhibitor use, n (%)		
≤12 months	161 (59)	166 (61)
>12 months	106 (39)	102 (38)
Unknown	5 (2)	3 (1)
Median prior chemotherapy regimens in the metastatic setting, n (range)[d]	3 (0-8)	3 (1-5)

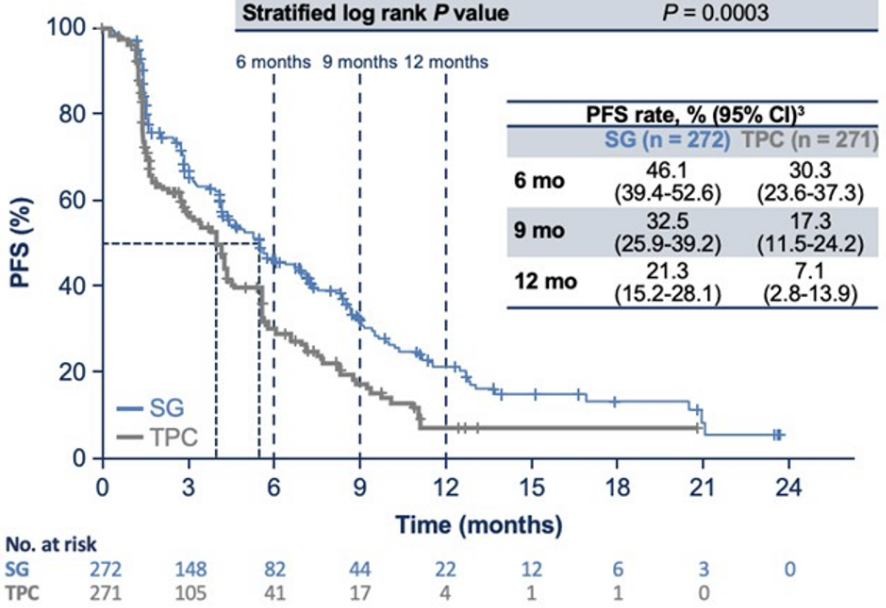
- TODOS LOS PACIENTES HABÍAN PROGRESADO A UN TRATAMIENTO PREVIO CON ICDK4/6.
- MEDIANA DE 3 REGIMENES DE TRATAMIENTO CON QUIMIOTERAPIA PREVIO

Tolaney, ASCO 2023

Resultados

PFS

BICR analysis	SG (n = 272)	TPC (n = 271)
Median PFS, mo (95% CI)	5.5 (4.2-7.0)	4.0 (3.1-4.4)
Stratified HR (95% CI)	**0.66** (0.53-0.83)	
Stratified log rank *P* value	*P* = 0.0003	



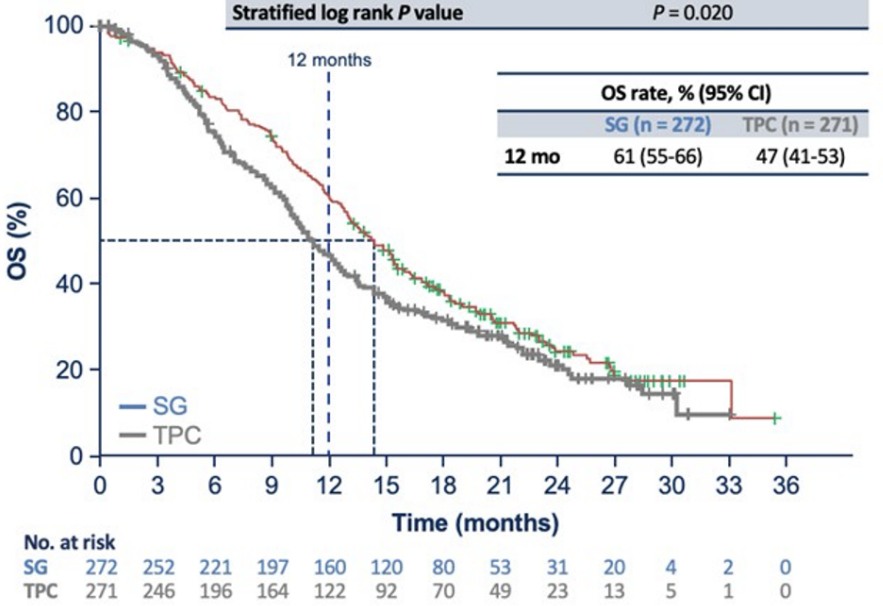
PFS rate, % (95% CI)[3]	SG (n = 272)	TPC (n = 271)
6 mo	46.1 (39.4-52.6)	30.3 (23.6-37.3)
9 mo	32.5 (25.9-39.2)	17.3 (11.5-24.2)
12 mo	21.3 (15.2-28.1)	7.1 (2.8-13.9)

No. at risk									
SG	272	148	82	44	22	12	6	3	0
TPC	271	105	41	17	4	1	1	0	

Median follow-up was 10.2 months.

OS

	SG (n = 272)	TPC (n = 271)
Median OS, mo (95% CI)	14.4 (13.0-15.7)	11.2 (10.1-12.7)
Stratified HR (95% CI)	**0.79** (0.65-0.96)	
Stratified log rank *P* value	*P* = 0.020	



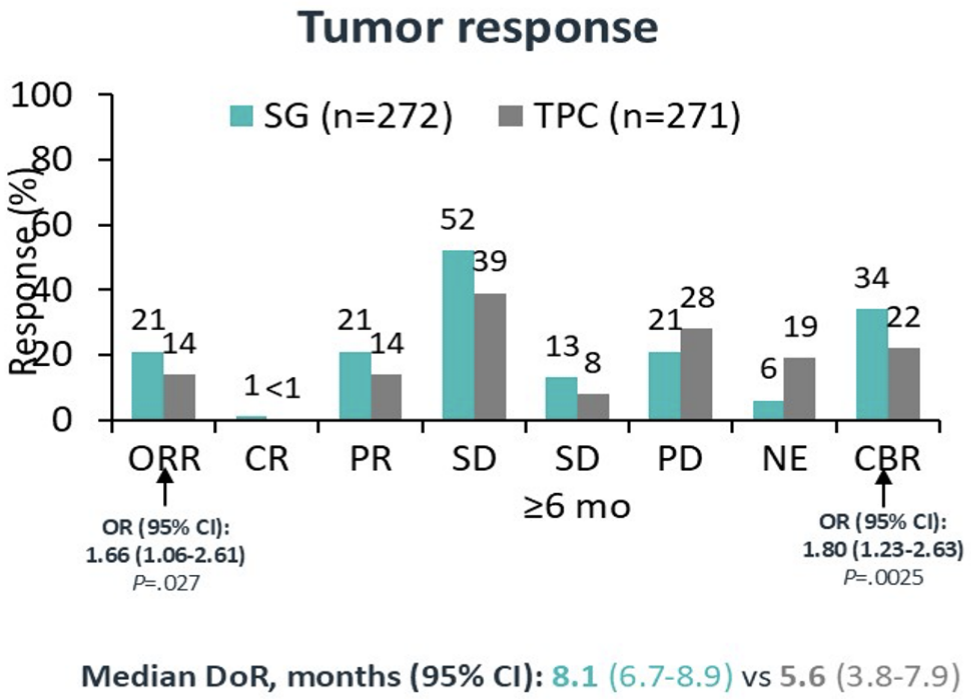
OS rate, % (95% CI)	SG (n = 272)	TPC (n = 271)
12 mo	61 (55-66)	47 (41-53)

No. at risk													
SG	272	252	221	197	160	120	80	53	31	20	4	2	0
TPC	271	246	196	164	122	92	70	49	23	13	5	1	0

Median follow-up was 12.5 months.

1Rugo HS, et al. *J Clin Oncol*. 2022;40:3365-3376.
Rugo HS, et al. *Lancet*. 2023;402:1423-1433.
Rugo, HS, et al. Presented at: 2022 ASCO Annual Meeting; June 3-7, 2022; Chicago, IL. LBA1001.

Respuesta y seguridad TROPICS-02



Median DoR, months (95% CI): 8.1 (6.7-8.9) vs **5.6** (3.8-7.9)

Safety summary

n (%)		SG (n=268)		TPC (n=249)	
AE Grade ≥3		199 (74)		149 (60)	
AEs → discontinuation		17 (6)		11 (4)	
AEs → dose delay		178 (66)		109 (44)	
AEs → dose reductions		91 (34)		82 (33)	
SAEs		74 (28)		48 (19)	
AEs → death[a]		6 (2)		0	
		Any grade	Grade ≥3	Any grade	Grade ≥3
Hematologic	Neutropenia	189 (71)	140 (52)	136 (55)	97 (39)
	Anemia	98 (37)	20 (7)	69 (28)	8 (3)
	Thrombocytopenia	17 (6)	1 (<1)	41 (16)	9 (4)
GI	Diarrhea	166 (62)	27 (10)	57 (23)	3 (1)
	Nausea	157 (59)	3 (1)	87 (35)	7 (3)
	Constipation	93 (35)	1 (<1)	61 (24)	0
	Vomiting	64 (24)	3 (1)	39 (16)	4 (2)
	Abdominal pain	53 (20)	10 (4)	34 (14)	2 (1)
Other	Alopecia	128 (48)	0	46 (18)	0
	Fatigue	105 (39)	16 (6)	82 (33)	9 (4)
	Asthenia	62 (23)	6 (2)	50 (20)	5 (2)
	Decreased appetite	57 (21)	4 (1)	52 (21)	2 (1)
	Dyspnea	49 (18)	5 (2)	39 (16)	11 (4)
	Headache	44 (16)	1 (<1)	36 (14)	2 (1)
	Pyrexia	39 (15)	2 (1)	45 (18)	0
	AST increased	33 (12)	4 (1)	44 (18)	8 (3)

[a]Of 6 AEs leading to death, 1 (septic shock due to neutropenic colitis) was considered treatment related by investigator

Rugo HS et al. *J Clin Oncol*. 2022;40(29):3365-3376. Rugo HS et al. 2022 ESMO Congress. Abstract 1553O. Rugo HS et al. 2022 SABCS. Abstract GS1-11.Tolaney et al. 2023 ASCO Annual Meeting. Abstract 1003. Rugo HS et al. *Lancet*. 2023;402(10411):1423-1433.

TROPION-Breast01: Datopotamab deruxtecan vs QT para cáncer de mama Luminal IV

Key eligibility

- HR+/HER2−[a] breast cancer
- Previously treated with 1–2 lines of chemo (inoperable/metastatic setting)
- Experienced progression on ET and for whom ET was unsuitable
- ECOG PS 0/1

R 1:1

Dato-DXd
6 mg/kg IV Day 1 Q3W
(n=365)

TPC[b]
(n=367)

Continue until PD, unacceptable toxicity / other discontinuation criteria

Dual primary endpoints[c]:

- PFS by BICR
- OS

Key secondary endpoint:

- ORR
- PFS (investigator assessed)
- Safety

Stratification factors

- Lines of chemo in unresectable/ metastatic setting (1 vs 2)
- Geographical location (US/Canada/ Europe vs ROW)
- Previous CDK4/6 inhibitor (yes vs no)

- At data cutoff (July 17, 2023), patients remaining on treatment:
  - Data-DXd, n=93
  - TPC, n=39
- Median follow-up: 10.8 months
- Median one line of prior therapy

[a]IHC 0/1+/2+; ISH−; [b]Investigator's choice of chemotherapy; [c]By BICR per RECIST v1.1.
Dato-DXd, datopotamab deruxtecan; TPC, treatment of physician's choice.

Bardia et al. SABCS 2023

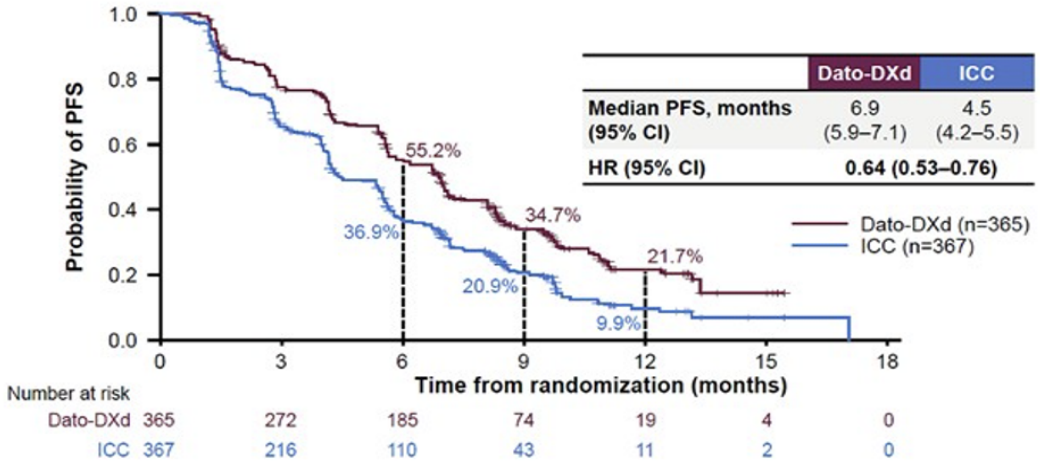
Población

		Dato-DXd (n=365)	ICC (n=367)
Age, median (range), years		56 (29–86)	54 (28–86)
Female, n (%)		360 (99)	363 (99)
Race, n (%)	Black or African American / Asian / White / Other*	4 (1) / 146 (40) / 180 (49) / 35 (10)	7 (2) / 152 (41) / 170 (46) / 38 (10)
Ethnicity, n (%)	Hispanic or Latino / Not Hispanic or Latino†	40 (11) / 322 (88)	43 (12) / 318 (87)
Prior lines of chemotherapy,‡ n (%)	1 / 2	229 (63) / 135 (37)	225 (61) / 141 (38)
Prior CDK4/6 inhibitor, n (%)	Yes / No	304 (83) / 61 (17)	300 (82) / 67 (18)
Prior taxanes and anthracyclines, n (%)	Taxane / Anthracycline	295 (81) / 228 (62)	296 (81) / 239 (65)
HER2 status at baseline by local testing,¶ n (%)	HER2 IHC 0	113 (31)	101 (28)
	HER2 IHC 1+, 2+ & FISH–	153 (42)	150 (41)

*Including not reported. †Ethnicity missing: 3 patients in Dato-DXd group; 6 patients in ICC group. ‡In the inoperable/metastatic setting; one patient in the Dato-DXd group had 3 prior lines of chemotherapy; one patient in the ICC group had 4 prior lines. ¶Latest known HER2 status (determined at diagnosis or at metastasis). All patients were required to have HER2-negative disease per ASCO/CAP guidelines, and qualitative results (i.e. negative HER2) could be reported. Quantitative HER2 value was missing in 99 patients (27%) in the Dato-DXd group and 116 patients (32%) in the ICC group.

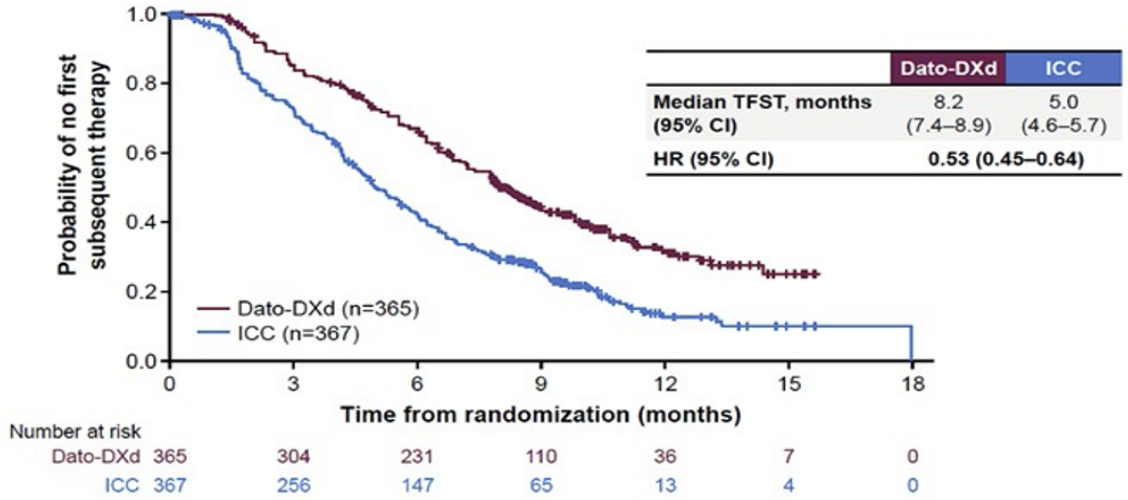
TROPION-Breast01: PFS y tiempo a siguiente tratamiento

PFS by investigator assessment



	Dato-DXd	ICC
Median PFS, months (95% CI)	6.9 (5.9–7.1)	4.5 (4.2–5.5)
HR (95% CI)	0.64 (0.53–0.76)	

Time to subsequent therapy



	Dato-DXd	ICC
Median TFST, months (95% CI)	8.2 (7.4–8.9)	5.0 (4.6–5.7)
HR (95% CI)	0.53 (0.45–0.64)	

PFS by BICR (primary endpoint)

- Median 6.9 vs 4.9 months
- HR 0.63 (95% CI: 0.52, 0)

Prior duration of CDK4/6i, ≤12 months

	Dato-DXd (n=151)	ICC (n=136)
Median PFS (95% CI), months	6.9 (5.5, 8.1)	4.2 (4.0, 5.5)
HR (95% CI)	0.61 (0.45, 0.81)	

Prior duration of CDK4/6i, >12 months

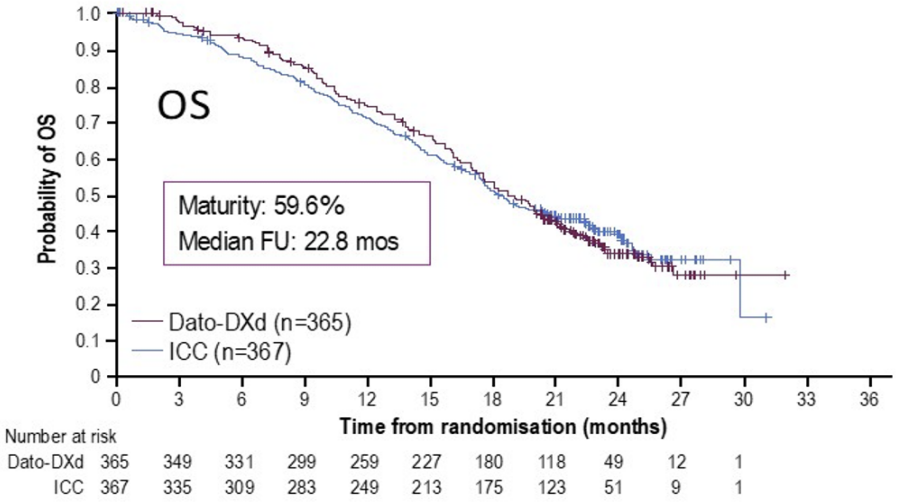
	Dato-DXd (n=153)	ICC (n=164)
Median PFS (95% CI), months	7.1 (5.8, 8.5)	5.0 (4.1, 5.7)
HR (95% CI)	0.61 (0.45, 0.82)	

Bardia A, et al. SABCS 2023. Abstract GS02-01; Bardia A, et al. J Clin Oncol 2025;43:285–96;

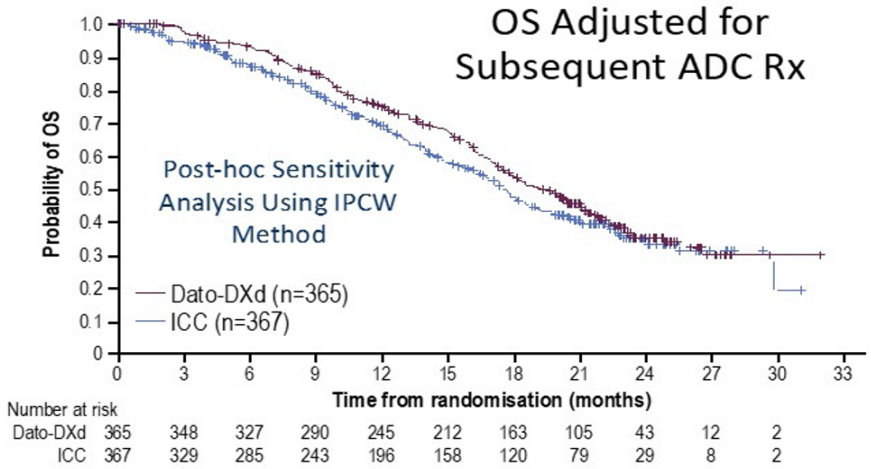
SG y siguientes tratamientos

- El uso de ADC como tratamiento tras discontinuación del estudio no estaba balanceado entre Dato y tratamiento estándar

- 74 vs. 79% recibieron tratamiento posterior; 12 vs. 24% recibieron ADC, la mayoría T-DXd



	Dato-DXd	ICC
OS events, n (%)	223 (61)	213 (58)
Median OS, months (95% CI)	18.6 (17.3–20.1)	18.3 (17.3–20.5)
HR (95% CI)	**1.01 (0.83–1.22)**	



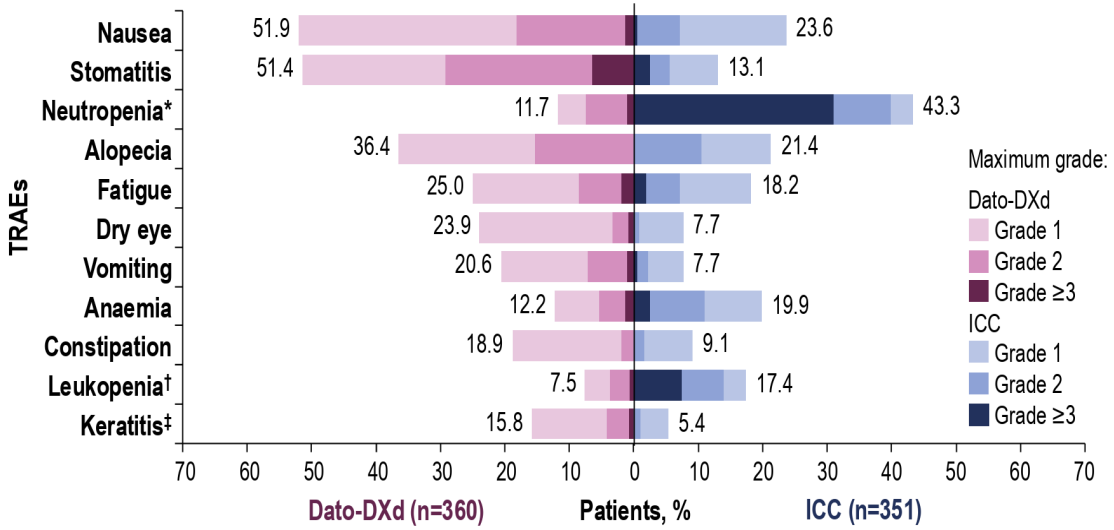
	Dato-DXd	ICC
OS events, n (%)	195 (53)	177 (48)
Median OS, months	19.1	17.5
HR (95% CI)	0.86 (0.70–1.06)	

Data cutoff: 24 July 2024.

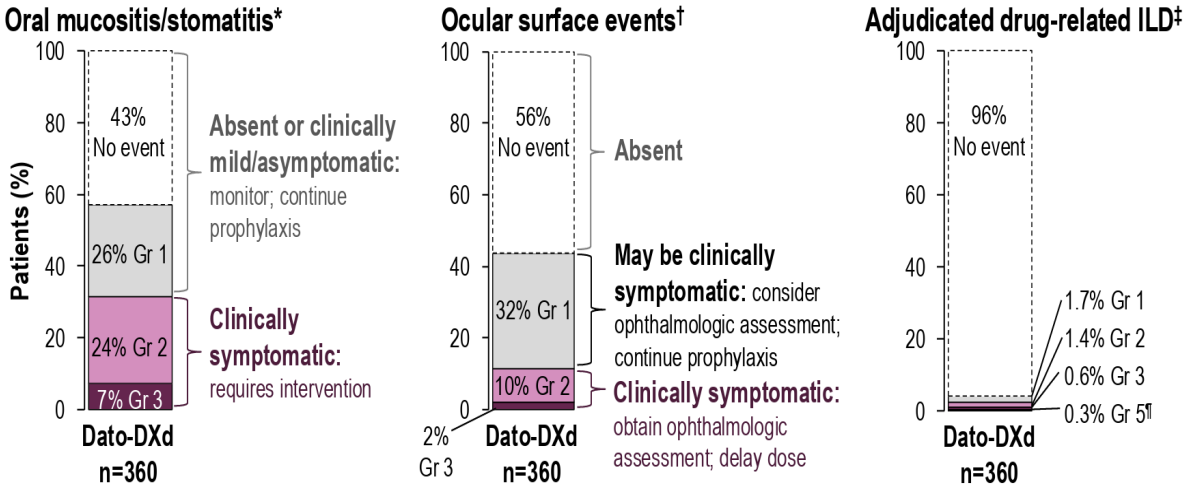
Pistilli et al, ESMO Virtual Plenary February 12, 2025

Seguridad

TRAEs Occurring in ≥15% of Patients



Treatment-Related AESIs for Dato-DXd



- Oral mucositis/stomatitis events were recovered/resolved or recovering/resolving in 178/206 patients (86%)
- Grade 3 ocular surface events were either recovered/resolved or recovering/resolving in 6/7 patients (86%)§

Tropion Breast06

TROPION-Breast06: Multicenter, multinational, open-label, single-arm, phase 3b study of datopotamab deruxtecan (Dato-DXd) in patients with locally advanced inoperable or metastatic HR+/HER2 IHC 0 breast cancer refractory to endocrine therapy

Komal L. Jhaveri,[1,2] Ana C. Garrido-Castro,[3,4] Adrien Decque,[5] Flavia Lujan,[5] Manoj Prahladan,[5] Rosemary Taylor,[6] Nikki Toms,[5] François-Clément Bidard[7]

[1]Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA; [2]Department of Medicine, Weill Cornell Medical College, New York, NY, USA; [3]Department of Medical Oncology, Dana-Farber Cancer Center Institute, Boston, MA, USA; [4]Harvard Medical School, Boston, MA, USA; [5]Global Medical Affairs, AstraZeneca, Cambridge, UK; [6]Oncology Biometrics, Oncology R&D, AstraZeneca, Macclesfield, UK; [7]Department of Medical Oncology, Institute Curie, Paris and Saint-Cloud, France

Poster PS5-07-21

ePosters

Plain language summary

Why are we performing this research?

- Patients with hormone receptor (HR)-positive/human epidermal growth factor receptor 2 (HER2)-negative breast cancer may have tumors with no HER2 expression (also known as immunohistochemistry [IHC] 0), or tumors with a small amount of HER2 expression (HER2-low). For those with HER2 IHC 0, who no longer respond to hormone therapy, treatment options are limited.[1,2]
- Datopotamab deruxtecan (Dato-DXd) is an antibody-drug conjugate, which is a chemotherapy (DXd) joined to an antibody (datopotamab), connected via a cleavable linker.[3] Based on results from the TROPION-Breast01 study, Dato-DXd is approved for the treatment of patients with HR-positive/HER2-negative breast cancer (including patients with tumors that have no HER2 expression and those with a small amount of HER2 expression) that had spread (i.e. were metastatic), who had already received chemotherapy and hormone therapy.[4,5]
- In the TROPION-Breast01 study, Dato-DXd was effective, slowed down cancer progression and had manageable side effects.[6]
- Building upon these results, this study, known as TROPION-Breast06, will assess Dato-DXd in patients with HR-positive/HER2 IHC 0 breast cancer, that cannot be treated with surgery or is metastatic, who have not received prior chemotherapy, and whose tumor no longer responds to hormone therapy.

How are we performing this research?

Approximately 100 patients will receive Dato-DXd through an intravenous injection every three weeks. Patients will be monitored for how well the treatment controls the cancer, how long it works, and what side effects occur.

Who will participate in this study?

Eligible patients enrolled into this study:

- Have HR-positive/HER2 IHC 0 breast cancer that cannot be treated with surgery or is metastatic.
- Have tried hormone therapy but it no longer works.
- Have not received chemotherapy or antibody-drug conjugates for metastatic breast cancer.

Where can I access more information?

For more information about TROPION-Breast06, please visit https://clinicaltrials.gov/study/NCT07205822.
You may also speak to your doctor about clinical studies.

1. Tolaney SM, et al. ESMO Open 2024;9:103691. 2. Chaintikun S, et al. Breast Cancer Res Treat 2020;183:729–39. 3. Okajima D, et al. Mol Cancer Ther 2021;20:2329–40. 4. US FDA. DATROWAY® Prescribing Information 2025. 5. EMA. DATROWAY® Summary of Product Characteristics 2025. 6. Bardia A, et al. J Clin Oncol 2024;43:285–96.

Background

- Patients with endocrine-refractory HR+/HER2− (IHC 0, IHC 1+, or IHC 2+/ISH−) metastatic breast cancer have limited treatment options; while CT is a mainstay of treatment, limited efficacy contributes to poor patient outcomes and highlights the need for more durable and effective therapeutic options.[1,2]
- Dato-DXd is a TROP2-directed ADC composed of a humanized anti-TROP2 IgG1 monoclonal antibody conjugated to a highly potent topoisomerase I inhibitor payload via a tetrapeptide-based, tumor-selective cleavable linker.[3]
- Dato-DXd is approved in multiple countries for the treatment of adults with unresectable or metastatic HR+/HER2− (IHC 0, IHC 1+, or IHC 2+/ISH−) breast cancer who have received prior ET and CT for unresectable or metastatic disease, based on the results of the phase 3 TROPION-Breast01 study.[4–6]
  - In this study, treatment with Dato-DXd reduced the risk of disease progression or death by 37% compared with CT (hazard ratio, 0.63 [95% CI, 0.52–0.76]; p<0.0001). Median PFS by BICR was 6.9 months with Dato-DXd versus 4.9 months with CT and Dato-DXd demonstrated a manageable safety profile.[4]
- In the phase 3 DESTINY-Breast06 study, the HER2-directed ADC, trastuzumab deruxtecan, significantly improved outcomes compared with CT in patients with HR+/HER2-low (IHC 1+ or IHC 2+/ISH−) or HER2-ultralow (IHC 0 with membrane staining) unresectable or metastatic breast cancer.[7]
- TROPION-Breast06 aims to build upon the results of TROPION-Breast01, by assessing the efficacy and safety of Dato-DXd in the endocrine-refractory setting prior to CT for patients with HR+/HER2 IHC 0 (defined as no staining or incomplete and faint/barely perceptible membrane staining in ≤10% of tumor cells) inoperable or metastatic breast cancer.

TROPION-Breast06 (NCT07205822): An open-label, single-arm, phase 3b study

- HR+/HER2 IHC 0* locally advanced inoperable or metastatic breast cancer
- Progressed on and not suitable for further ET
- No prior treatment with any TROP2-targeted therapy or any agent targeting Topo-I (including ADCs)
- No prior CT for metastatic breast cancer

→ N≈100 → Dato-DXd 6 mg/kg IV Q3W†

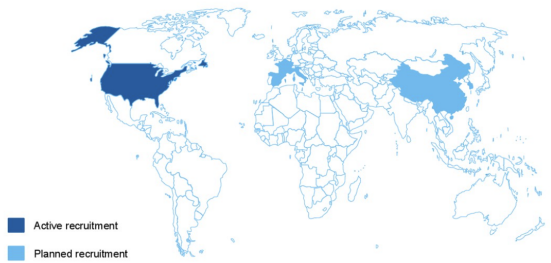
Primary Endpoint

Investigator-assessed PFS per RECIST v1.1

- A daily oral care plan for oral mucositis/stomatitis prophylaxis will be given to all patients
- Patients will complete daily diaries to collect information about oral care and adherence to prophylaxis and symptom severity
- Prophylaxis for ocular surface events will be strongly advised

*As per ASCO/CAP guidelines on local laboratory results. HR+ defined as: either ER and/or PgR positive (ER or PgR ≥1%); HER2 IHC 0 defined as: no staining or incomplete and faint/barely perceptible membrane staining in ≤10% of tumor cells.[8,9]
†Participants will receive study intervention until RECIST v1.1-defined radiological progression by investigator, unacceptable toxicity or the patient withdraws from the study.

Enrollment start: October 2025 | Enrollment is ongoing



Countries with participating study sites (~40 sites)

China, France, Italy, Republic of Korea, Spain, USA

Key inclusion criteria

- Age ≥18 years with inoperable or metastatic HR+/HER2 IHC 0 breast cancer per ASCO/CAP guidelines by local testing[8,9]
  - HR+ defined as: either ER and/or PgR positive (ER or PgR ≥1%)
  - HER2 IHC 0 defined as: no staining or incomplete and faint/barely perceptible membrane staining in ≤10% of tumor cells
- Progressed on and not suitable for further ET per investigator assessment
- ECOG PS 0 or 1
- Measurable disease per RECIST v1.1; baseline biopsy mandatory (archival samples are permitted if obtained no earlier than 6 weeks prior to screening; bone biopsies are not permitted)
- Adequate bone marrow reserve and organ function within 7 days prior to first dose of study treatment

Key exclusion criteria

- Evidence of severe or uncontrolled systemic diseases
  - Including active bleeding diseases and significant cardiac or psychological conditions
- History of allogenic organ transplant
- History of substance abuse
- Persistent toxicities caused by previous anticancer therapy, excluding alopecia, not yet improved to grade ≤1 or baseline
- Spinal cord compression or brain metastases unless treated, no longer symptomatic and radiologically stable
- Leptomeningeal carcinomatosis or metastasis
- Clinically significant corneal disease
- Active infection with hepatitis B or C, HIV or tuberculosis
- Suspected, current or history of non-infectious ILD/pneumonitis that required steroids or other severe pulmonary function compromise
- Prior exposure to TROP2-targeted therapy, any treatment (including ADC) with a Topo-I-targeted therapy or any chemotherapy in the metastatic setting
- Contraindication to the use of steroid-containing mouthwash

Key study endpoints

1° Primary endpoint

- Investigator-assessed PFS per RECIST v1.1

2° Secondary endpoints

- Proportion of patients with oral mucositis/stomatitis, ocular surface events and treatment-related grade ≥3 adverse events
- CBR
  - Proportion of patients with a confirmed CR or PR or who have SD per RECIST 1.1 (investigator-assessed) for at least 24 weeks following first dose of study treatment
- ORR
- DoR
- OS
- Safety and tolerability

Poster

Abbreviations

ADC, antibody-drug conjugate; ASCO, American Society of Clinical Oncology; BICR, blinded independent central review; CAP, College of American Pathologists; CBR, clinical benefit rate; CI, confidence interval; CT, chemotherapy; CR, complete response; Dato-DXd, datopotamab deruxtecan; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; ER, estrogen receptor; ET, endocrine therapy; HER2−, human epidermal growth factor receptor 2-negative; HIV, human immunodeficiency virus; HR+, hormone receptor-positive; IgG1, immunoglobulin G1; IHC, immunohistochemistry; ILD, interstitial lung disease; ISH, in situ hybridization; IV, intravenous; ORR, objective response rate; OS, overall survival; OSE, ocular surface events; PFS, progression-free survival; PR, partial response; PgR, progesterone receptor; Q3W, every three weeks; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SD, stable disease; Topo-I, topoisomerase I; TROP2, trophoblast cell surface protein-2.

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Disclosures

Komal Jhaveri reports consultant/advisory board role for Arvinas, AstraZeneca, Bicycle Therapeutics, Blueprint Medicines, Daiichi Sankyo, Eisai, Genentech, Gilead, Halda Therapeutics, Lilly/Loxo Oncology, Menarini/Stemline, Merck Pharmaceuticals, Novartis, Olema Pharmaceuticals, Pfizer, Rayzebio, Scorpion Therapeutics and Zymeworks, and research funding support (Institution) from AstraZeneca, Bicycle Therapeutics, Blueprint Medicines, BridgeBio Oncology Therapeutics, Eisai, Genentech, Gilead, Lilly/Loxo Oncology, Merck Pharmaceuticals, Novartis, Pfizer, PUMA Biotechnology, Rayzebio, Scorpion Therapeutics and Zymeworks.

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ASCENT 07

SAN ANTONIO BREAST CANCER SYMPOSIUM® · UT Health San Antonio Mays Cancer Center · AACR American Association for Cancer Research
DECEMBER 9–12, 2025
HENRY B. GONZALEZ CONVENTION CENTER • SAN ANTONIO, TX

Sacituzumab Govitecan vs Chemotherapy as First Therapy After Endocrine Therapy in HR+/HER2− (IHC 0, 1+, 2+/ISH−) Metastatic Breast Cancer: Primary Results From ASCENT-07

Komal Jhaveri [1,2], Yeon Hee Park[3], Carlos Barrios[4], Giuseppe Curigliano[5,6], Hiroji Iwata[7], Javier Cortés[8-10], Delphine Loirat[11], Tomás Pascual[12-15], Zhimin Shao[16,17], Carlos Gallardo Araneda[18], Toshinari Yamashita[19], Marta Tapia[20,21], Pelin Cinar[22], Sivuonthuon Lam[22], Xuehan Ren[22], Wendy Verret[22], Joyce Kwan[22], Kevin Punie[23], Hope S Rugo[24]

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WEDNESDAY, December 10, 2025, 11:30 AM–11:45 PM - GS1-09

ASCENT-07: Phase 3, Randomized, Open-Label Study

Locally advanced unresectable or metastatic HR+/HER2− BC:

- **No prior chemotherapy** for locally advanced or metastatic HR+/HER2− BC
- Measurable disease per RECIST v1.1
- Must have at least 1 of the following:
  - Progression on ≥ 2 previous lines of ET ± targeted therapy for mBC[a]
  - Progression < 6 mo of starting 1L ET ± CDK4/6i for mBC
  - Recurrence < 24 mo of starting adjuvant ET + CDK4/6i and no longer a candidate for additional ET for mBC

N = 690
R 2:1

Sacituzumab govitecan 10 mg/kg IV Days 1 and 8, every 21 days n = 456

Treatment of physician's choice (capecitabine, paclitaxel, nab-paclitaxel)[b] n = 234

Treatment continued until disease progression[c] or unacceptable toxicity

Stratification factors:

- Duration of prior CDK4/6i[d] for mBC (none vs ≤ 12 mo vs > 12 mo)
- HER2 IHC (HER2 IHC 0 vs HER2 IHC-low [IHC 1+ or IHC 2+/ISH–])
- Geographic region (US/Canada/UK/EU vs ROW)

End points

Primary
- PFS by BICR

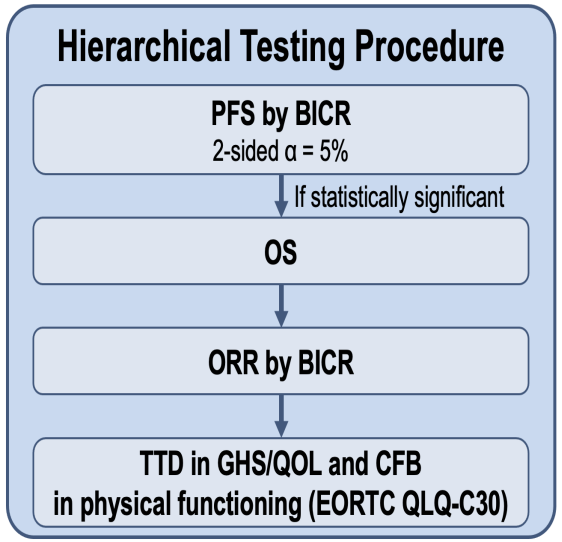
Key Secondary
- OS
- ORR by BICR
- QOL

Other Secondary
- PFS by INV
- ORR by INV
- DOR by BICR and INV
- Safety

ClinicalTrials.gov identifier: NCT05840211.
[a]Disease recurrence while on the first 24 months of starting adjuvant ET will be considered a line of therapy; these participants will only require 1 line of ET in the metastatic setting. [b]Paclitaxel 80 mg/m² or nab-paclitaxel 100 mg/m² IV on days 1, 8, and 15 of 28-day cycles, or capecitabine oral 1000 or 1250 mg/m² twice daily for first 2 weeks of 21-day cycles. [c]Per RECIST v1.1. [d]Enrollment of CDK4/6i-naïve participants was capped at 10%.
1L, first-line; **BICR**, blinded independent central review; **CDK4/6i**, cyclin-dependent kinase 4/6 inhibitor; **DOR**, duration of response; **ET**, endocrine therapy; **EU**, European Union; **HER2−**, human epidermal growth factor receptor 2 negative; **HR+**, hormone receptor positive; **IHC**, immunohistochemistry; **INV**, investigator assessment; **ISH**, in situ hybridization; **IV**, intravenously; **mBC**, metastatic breast cancer; **mo**, months; **ORR**, objective response rate; **OS**, overall survival; **PFS**, progression-free survival; **QOL**, quality of life; **R**, randomized; **RECIST v1.1**, Response Evaluation Criteria in Solid Tumors, version 1.1; **ROW**, rest of the world.

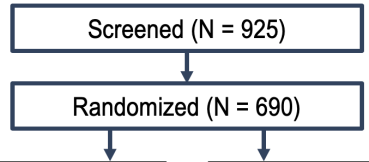
Statistical Analysis

- Planned enrollment: ~654 participants (actual enrolled: 690)
- Data cutoff for primary PFS analysis (planned after ~415 events): September 15, 2025
  - 419 observed PFS events by BICR (61% maturity)
  - 187 observed OS events (27% maturity)
- The study had 99% power to detect a PFS HR of 0.64 at two-sided 5% significance level (MDD HR=0.815)
- Median duration of follow-up: 15.4 months



BICR, blinded independent central review; **CFB**, change from baseline; **EORTC QLQ-C30**, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30; **GHS**, Global Health Status; **HR**, hazard ratio; **MDD**, minimum detectable difference; **ORR**, objective response rate; **OS**, overall survival; **PFS**, progression-free survival; **QOL**, quality of life; **TTD**, time to deterioration.

Participant Disposition



n (%)	SG (n = 456)
Treated	449 (98)
Discontinued study treatment	348 (76)
Disease progression	301 (66)
Adverse events	14 (3)
Participant decision	12 (3)
Death	10 (2)
Never dosed with study drug	7 (2)
Investigator decision	4 (1)
Lost to follow-up	1 (< 1)

n (%)	TPC (n = 234)
Treated	232 (99)
Discontinued study treatment	203 (87)
Disease progression	164 (70)
Adverse events	15 (6)
Death	9 (4)
Investigator decision	9 (4)
Participant decision	4 (2)
Never dosed with study drug	2 (1)
Lost to follow-up	0 (0)

- Capecitabine (43%)
- Taxane (57%)
  - Nab-paclitaxel (39%)
  - Paclitaxel (18%)

At data cutoff[a], 139 (20%) participants remained on treatment: 108 (24%) on SG and 31 (13%) on TPC

[a]September 15, 2025.
SG, sacituzumab govitecan; **TPC**, treatment of physician's choice.

Demographics and Baseline Characteristics

ITT Population	SG (n = 456)	TPC (n = 234)
Female sex, n (%)	452 (99)	232 (99)
Median age, (range) year	57 (29-88)	58 (27-80)
≥ 65 years, n (%)	106 (23)	74 (32)
Geographic region[a], n (%)		
US/Canada/UK/EU	181 (40)	93 (40)
Rest of the world	275 (60)	141 (60)
Race[b], n (%)		
White	227 (50)	106 (45)
Asian	176 (39)	95 (41)
Black	10 (2)	3 (1)
Other/Not specified	43 (9)	30 (13)
ECOG PS at baseline[c], n (%)		
0	269 (59)	145 (62)
1	187 (41)	89 (38)

ITT Population	SG (n = 456)	TPC (n = 234)
ER/PR status[d], n (%)		
ER+ and PR+	286 (63)	165 (71)
ER+ and PR−	164 (36)	66 (28)
ER− and PR+	2 (<1)	2 (1)
HER2 expression[d,e], n (%)		
IHC 0	192 (42)	100 (43)
HER2 low (IHC 1+; IHC2+/ISH-)	264 (58)	134 (57)
Primary endocrine resistance[f], n (%)	143 (31)	62 (26)
Time from metastatic diagnosis to randomization, median (range) months	23.9 (0.5-192.0)	26.2 (0.3-152.1)
De novo metastatic disease at diagnosis, n (%)	111 (24)	48 (21)
Visceral disease, n (%)	407 (89)	205 (88)
Liver metastasis n (%)	320 (70)	156 (67)
Brain metastasis, n (%)	18 (4)	14 (6)
Bone-only disease, n (%)	18 (4)	11 (5)

[a]EU includes Austria, Belgium, Czech Republic, France, Germany, Greece, Hungary, Italy, Poland, Portugal, and Spain; rest of the world includes Argentina, Australia, Brazil, Chile, China, Hong Kong, Israel, Japan, Malaysia, Mexico, Republic of Korea, Singapore, South Africa, and Taiwan. [b]As reported by the participants; Other/Not specified includes American Indian or Alaska Native, other races, and not provided/collection not permitted. [c]Scores range from 0 to 5, with higher scores indicating greater disability. [d]Per local testing. [e]Per IRT. [f]Primary endocrine resistance was defined as relapse that had occurred during the first 2 years of adjuvant endocrine therapy or progressive disease that had occurred during the first 6 months of first-line endocrine therapy for metastatic breast cancer.
ECOG PS, Eastern Cooperative Oncology Group performance status; **ER**, estrogen receptor; **EU**, European Union; **HER2**, human epidermal growth factor receptor 2; **IHC**, immunohistochemistry; **IRT**, interactive response technology; **ISH**, in situ hybridization; **ITT**, intent-to-treat; **PR**, progesterone receptor; **SG**, sacituzumab govitecan; **TPC**, treatment of physician's choice.

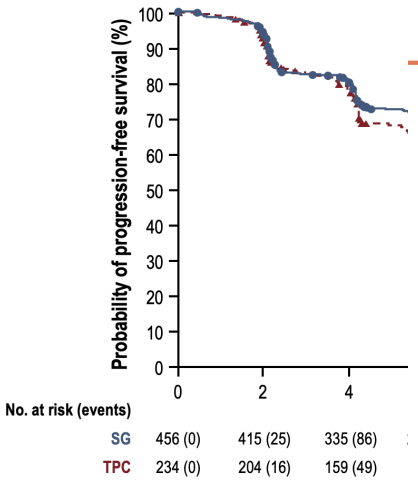
Prior Therapies

ITT Population	SG (n = 456)	TPC (n = 234)
Metastatic setting		
Median number of lines (range)	2 (0-8)	2 (0-4)
Lines of ET, n (%)		
None	8 (2)	1 (<1)
1 line	122 (27)	63 (27)
2 lines	263 (58)	139 (59)
≥ 3 lines	63 (14)	31 (13)
Previous endocrine-based therapies[a], n (%)		
ET with CDK4/6i	416 (91)	216 (92)
ET with CDK4/6i ≤ 6 months[b]	74 (16)	35 (15)
ET monotherapy	182 (40)	95 (41)
ET with other targeted therapy[c]	160 (35)	74 (32)

ITT Population	SG (n = 456)	TPC (n = 234)
Adjuvant/neoadjuvant setting[a,d], n (%)		
ET[e]	295 (65)	158 (68)
ET with CDK4/6i	17 (4)	8 (3)
Chemotherapy	260 (57)	140 (60)
Taxane	211 (46)	115 (49)
Anthracycline	217 (48)	118 (50)
Prior CDK4/6i use in metastatic setting, n (%)		
None	32 (7)	19 (8)
≤ 12 months	197 (43)	98 (42)
> 12 months	227 (50)	117 (50)

[a]Therapies reported are not mutually exclusive. [b]In first line. [c]Other targeted therapies in the SG and TPC groups included everolimus (25% and 22%), alpelisib (5% and 3%), and olaparib (2% and 3%). [d]Some participants had unknown adjuvant therapy history. [e]ET includes ET monotherapy and combination therapy.
CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; **ET**, endocrine therapy; **ITT**, intent-to-treat; **SG**, sacituzumab govitecan; **TPC**, treatment of physician's choice.

Primary End Point: P[illegible]



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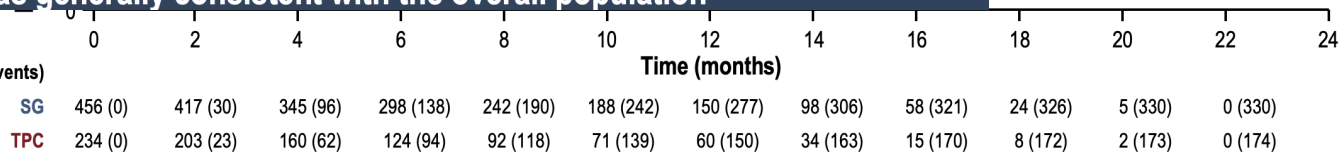
Subgroup Analysis of Progression-Free Survival by BICR

Prespecified subgroup	SG n	SG mPFS, mo	TPC n	TPC mPFS, mo	Unstratified HR (95% CI)
ITT population	456	8.3	234	8.3	0.88 (0.72-1.08)
Age group					
< 65 years	350	8.3	160	8.2	0.87 (0.68-1.10)
≥ 65 years	106	9.7	74	9.4	0.88 (0.59-1.30)
Geographic region					
US/Canada/UK/EU	181	8.3	93	8.3	1.00 (0.72-1.40)
Rest of the world	275	8.5	141	8.2	0.81 (0.63-1.05)
HER2 IHC status[a]					
HER2 IHC0	192	9.2	100	8.1	0.75 (0.55-1.02)
HER2 IHC low	264	8.2	134	8.4	1.00 (0.76-1.31)
Prior CDK4/6 inhibitor use in metastatic setting					
None	32	12.2	19	8.2	0.68 (0.32-1.44)
≤ 12 months	197	8.3	98	6.2	0.78 (0.57-1.06)
> 12 months	227	8.3	117	9.1	1.00 (0.74-1.34)
Received chemotherapy in neoadjuvant/adjuvant setting					
Yes	260	8.3	140	9.1	1.05 (0.80-1.37)
No	196	10.3	94	8.0	0.70 (0.51-0.95)
Choice of chemotherapy[b]					
Taxane (paclitaxel or nab-paclitaxel)	236	8.3	134	8.1	0.81 (0.62-1.07)
Capecitabine	220	8.5	100	9.4	1.00 (0.73-1.38)
Number of prior lines of ET in metastatic setting					
≤1	130	8.8	64	10.2	0.87 (0.58-1.30)
>1	326	8.3	170	8.1	0.88 (0.70-1.12)
Endocrine resistance					
Primary	143	10.2	62	8.4	0.79 (0.53-1.17)
Secondary	313	8.3	172	8.2	0.93 (0.73-1.19)
Liver metastases					
Yes	320	8.2	156	8.0	0.92 (0.72-1.18)
No	136	14.1	78	10.2	0.76 (0.52-1.11)

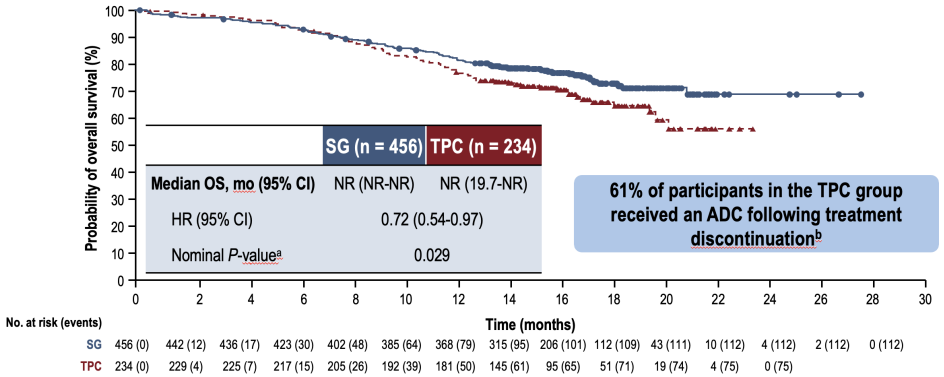
PFS among subgroups was generally consistent with the overall population

	SG (n = 456)	TPC (n = 234)
(95% CI)	8.4 (8.2-9.7)	6.4 (6.0-8.1)
95% CI)	0.78 (0.64-0.93)	
ue[a]	0.008	
e, % (95% CI)	69 (64-73)	58 (51-64)
te, % (95% CI)	36 (32-41)	30 (24-36)



There was a numerical improvement in investigator-assessed PFS with SG versus TPC

Overall Survival at Primary Analysis (27% maturity)



	SG (n = 456)	TPC (n = 234)
Median OS, mo (95% CI)	NR (NR-NR)	NR (19.7-NR)
HR (95% CI)	0.72 (0.54-0.97)	
Nominal *P*-value[a]	0.029	

61% of participants in the TPC group received an ADC following treatment discontinuation[b]

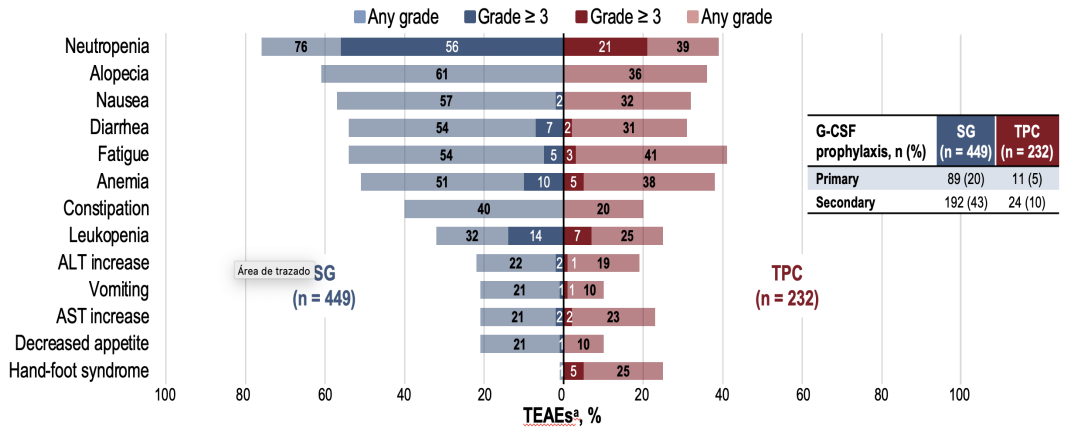
While the OS data were not mature, an early trend was observed favoring SG over TPC

Subsequent Anticancer Therapy

n (%)	SG (n = 348)	TPC (n = 203)
Participants without subsequent anticancer therapy[a]	66 (19)	43 (21)
Participants with any subsequent anticancer therapy[b]	282 (81)	160 (79)
ADC	91 (32)	97 (61)
T-DXd	83 (29)	66 (41)
SG	1 (0.4)	29 (18)
Dato-DXd	0	3 (2)
Other ADC	8 (3)	7 (4)
Chemotherapy	238 (84)	106 (66)
Targeted therapy[c]	65 (23)	24 (15)
Endocrine therapy	42 (15)	24 (15)
Immunotherapy	10 (4)	3 (2)
All other	5 (2)	3 (2)

Among participants who discontinued treatment, almost twice as many in the TPC group compared to the SG group received at least one subsequent ADC

Most Common (Occurring in ≥ 20%) Treatment-Emergent Adverse Events



G-CSF prophylaxis, n (%)	SG (n = 449)	TPC (n = 232)
Primary	89 (20)	11 (5)
Secondary	192 (43)	24 (10)

The most common grade ≥ 3 adverse events in both groups were neutropenia, leukopenia, and anemia

NCT04152499 (MK-2870-001): Study Design and Objectives[1-4]

Objectives: Phase 1/2, open-label, first in human study in China to evaluate sacituzumab tirumotecan (sac-TMT, formally MK-2870) as monotherapy in patients with locally advanced unresectable or metastatic solid tumors that are refractory to all standard therapies

Key Inclusion Criteria (N≈1300)

- Histologically or cytologically documented, incurable, locally advanced, recurrent or metastatic cancer
- Refractory to standard therapies or have no available standard therapy
- Confirmation of TROP2 expression by immunohistology or by other means was not required
- Measurable disease by CT/MRI
- ECOG PS, 0 or 1

Phase 1: Dose Escalation

Five dose levels: sac-TMT 2, 4, 6, 9, and 12 mg/kg

Phase 2: Dose Expansion

- Cohort 1: TNBC[a]
- Cohort 2: EOC
- Cohort 3A: NSCLC[b,c]
- Cohort 3B: EGFR WT NSCLC
- Cohort 4: GC/GEJC
- Cohort 5: ES SCLC
- Cohort 6: HR+/HER2−BC[c]
- Cohort 7: HNSCC
- Cohort 8: EC
- Cohort 9: UC

sac-TMT IV

Treatment will continue until disease progression or unacceptable toxicity

Primary Endpoints

- Phase 1: MTD and recommended doses for expansion
- Phase 2: ORR

Secondary Endpoints

- Phase 1: DLTs, safety, ORR, DOR, PFS, OS, ADA formation, PK[e] (C_{max})
- Phase 2: safety and tolerability, DOR, PFS, OS, ADA formation, PK[e] (half-life), levels of TROP2 expression in tumor tissue

[a]Patients in Cohort 1 (TNBC) were non-randomized and received MK-2870 4 mg/kg or 5 mg/kg IV Q2W. [b]Patients in Cohort 3A (NSCLC) and Cohort 6 (HR+/HER2− BC) received MK-2870 5 mg/kg IV Q2W. [c]Both patients with EGFR wild-type and EGFR mutant NSCLC were enrolled in the phase 2 expansion cohort. [e]PK parameters for MK-2870 –ADC, MK-2870 TAB, and free KL610023 payload.

1. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT04152499. Accessed: 14 January 2025. 2. Yin Y et al. Presented at SABCS 2022. 3. Fang W et al. Presented at ASCO 2023. 4. Ouyang et al. Presented at ESMO 2023.

(MK-2870-001): HR+/HER2- mBC Cohort

Efficacy Results

	All patients (N=38)[a]
ORR, n (%) Confirmed PR	14 (36.8) 12
DCR, n (%)	34 (89.5)
DOR Median (Range), months 6-month DOR rate, % (95% CI)	 7.4 (4.2~14.9+) 80.0 (40.9, 94.6)
PFS Median (95% CI), months 6-month PFS rate, % (95% CI)	 11.1 (5.4, 13.1) 61.2 (41.3, 76.1)
OS Median (95% CI), months 9-month OS rate (95% CI), %	 NE (10.71, NE) 81.4 (57.1, 92.7)

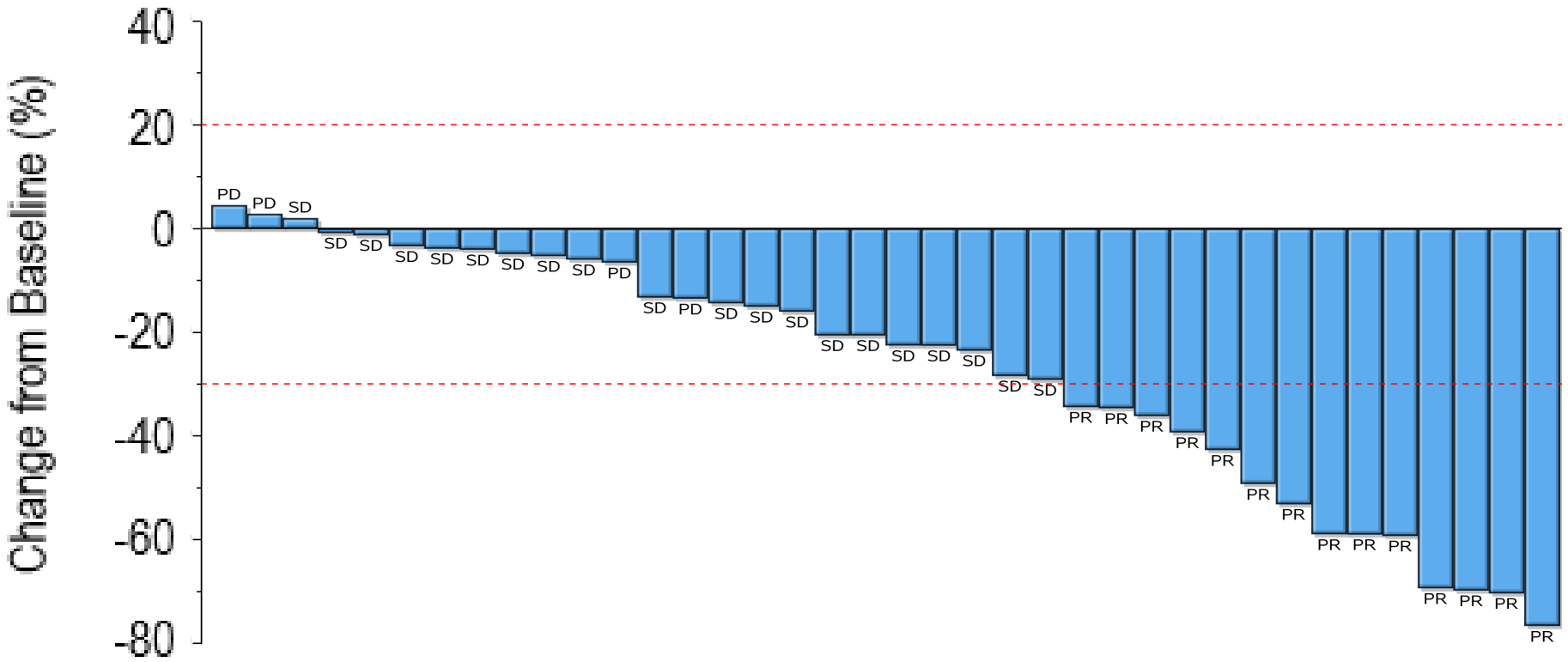
Data Cutoff Date: 12 April 2023. Median follow-up was 8.2 months.

[a]Of 41 patients were enrolled, 38 patients were evaluable for response assessment (defined as ≥1 on-study scan).

Ouyang et al. Presented at ESMO 2023.

(MK-2870-001): HR+/HER2- mBC Cohort

Best Change of Percentage in Target Lesion Size From Baseline per Investigator Assessment[1]



Data Cutoff Date: 12 April 2023. Median follow-up was 8.2 months. Ouyang et al. Presented at ESMO 2023.

(MK-2870-001): HR+/HER2- mBC Cohort

Safety

	SKB264 5mg/kg Q2W (N=41), n (%)	
	All Grade	≥Grade 3
TRAEs	41(100)	20(48.8)
TRAEs leading to dose reduction	7 (17.1)	5 (12.2)
TRAEs leading to dose delay	8 (19.5)	7 (17.1)
TRAEs leading to death	0	0
TRAEs in ≥25% any grade or ≥5% Grade >=3		
WBC decreased	35 (85.4)	9 (22.0)
Neutrophil count decreased	33 (80.5)	15 (36.6)
Anemia	33 (80.5)	6 (14.6)
Stomatitis	19 (46.3)	1 (2.4)
ALT increased	18 (43.9)	0
AST increased	17 (41.5)	0
Platelet count decreased	14 (34.1)	4 (9.8)
Rash	14 (34.1)	0
Blood LDH increased	13 (31.7)	0
GGT increased	12 (29.3)	3 (7.3)
Oropharyngeal pain	12 (29.3)	0
Lymphocyte count decreased	11 (26.8)	2 (4.9)

Data Cutoff Date: 12 April 2023. Median follow-up was 8.2 months.

1. Ouyang et al. Presented at ESMO 2023.

- The most common ≥ Grade 3 TRAEs (≥ 5%) was neutrophil count decreased, WBC decreased, anemia, platelet count decreased, and GGT increased
- No neuropathy or drug-related ILD/pneumonitis was reported. No TRAEs led to treatment discontinuation or death

OptiTROP-Breast02

BERLIN 2025 ESMO congress

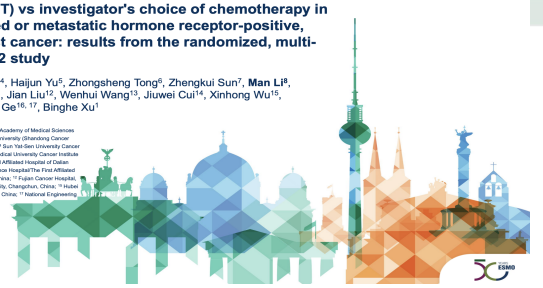
Sacituzumab tirumotecan (sac-TMT) vs investigator's choice of chemotherapy in previously treated locally advanced or metastatic hormone receptor-positive, HER2-negative (HR+/HER2-) breast cancer: results from the randomized, multi-center phase 3 OptiTROP-Breast02 study

Ying Fan[1], Huihui Li[2], Hao Wang[3], Shusen Wang[4], Haijun Yu[5], Zhongsheng Tong[6], Zhengkui Sun[7], **Man Li**[8], Xiying Shao[9], Yongmei Yin[10], Quchang Ouyang[11], Jian Liu[12], Wenhui Wang[13], Jiuwei Cui[14], Xinhong Wu[15], Gesha Liu[16], Yina Diao[16], Xiaoping Jin[16], Junyou Ge[16, 17], Binghe Xu[1]

[1] National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; [2] Cancer Hospital of Shandong First Medical University (Shandong Cancer Institute, Shandong Cancer Hospital), Jinan, China; [3] Sichuan Cancer Hospital, Chengdu, China; [4] Sun Yat-Sen University Cancer Center, Guangzhou, China; [5] Zhongnan Hospital of Wuhan University, Wuhan, China; [6] Tianjin Medical University Cancer Institute and Hospital, Tianjin, China; [7] Jiangxi Provincial Cancer Hospital, Nanchang, China; [8] The Second Affiliated Hospital of Dalian Medical University, Dalian, China; [9] Zhejiang Cancer Hospital, Hangzhou, China; [10] Jiangsu Province Hospital/The First Affiliated Hospital with Nanjing Medical University, Nanjing, China; [11] Hunan Cancer Hospital, Changsha, China; [12] Fujian Cancer Hospital, Fuzhou, China; [13] Weifang People's Hospital, Weifang, China; [14] The First Hospital of Jilin University, Changchun, China; [15] Hubei Cancer Hospital, Wuhan, China; [16] Sichuan Kelun-Biotech Biopharmaceutical Co., Ltd., Chengdu, China; [17] National Engineering Research Center of Targeted Biologics, Chengdu, China.

Presenter: Professor Man Li
The Second Affiliated Hospital of Dalian Medical University, Dalian, China

Sat, 18.10.2025



OptiTROP-Breast02 Study Design

Randomized, multi-center, open-lab

Key Eligibility

- HR+/HER2- BC*
- Prior 1 - 4 lines of chemotherapy
- At least one endocrine therapy, CDK
  inhibitor, and taxane in any setting

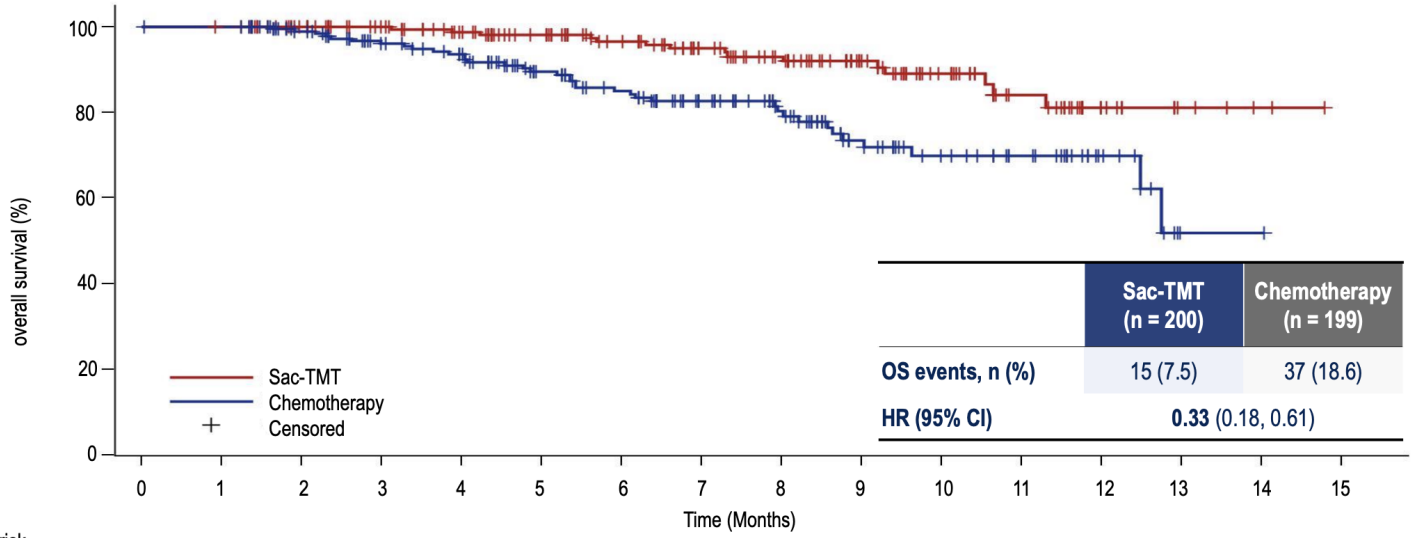
Stratification Factors:

1. Lines of chemotherapy (1 vs >1)
2. HER2 status (zero vs low) *
3. Endocrine therapy ≥ 6 months (yes vs no

*HER2- BC includes two subtypes: HER2-zero and HER2-lo
IHC2+/ISH-negative. † If no prior endocrine therapy in advanc
BC, breast cancer; BICR, blinded independent central revie
overall survival; Q2W, every 2 weeks; RECIST, Response E

Overall Survival

Positive OS trend observed with sac-TMT. The study continues to the pre-specified interim analysis for OS.



	Sac-TMT (n = 200)	Chemotherapy (n = 199)
OS events, n (%)	15 (7.5)	37 (18.6)
HR (95% CI)	**0.33** (0.18, 0.61)	

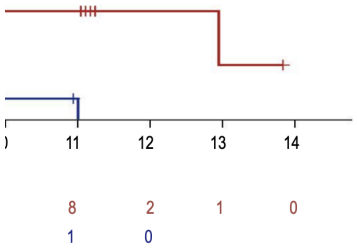
No.at risk

Sac-TMT	200	199	184	170	156	140	123	103	89	65	45	28	12	5	2	0
Chemotherapy	199	198	179	159	148	122	108	86	69	45	33	25	12	1	1	0

Median follow-up was 7.4 months

	Sac-TMT (n = 200)	Chemotherapy (n = 199)
	82 (41.0)	121 (60.8)
	8.3 (7.0, 8.6)	**4.1** (3.0, 4.3)
l)	**61.4** (52.9, 68.8)	**25.7** (18.2, 33.8)

R 0.35 (95% CI: 0.26, 0.48)
p* < 0.0001



The investigator-assessed PFS was consistent with BICR: HR 0.39 (95% CI: 0.30, 0.52)

* Based on pre-specified PFS IA, one-sided *P* value was less than the pre-specified efficacy boundary to achieve statistically significant improvement (one-sided alpha level of 0.010 determined by the O'Brien-Fleming alpha spending function).

TROFUSE 010

Key Eligibility Criteria

- Age ≥18 y
- Unresectable locally advanced or metastatic centrally confirmed HR+/HER2- breast cancer
- Disease recurrence on/after CDK4/6i (in the early or metastatic setting)
- ECOG PS 0 or 1
- No prior chemotherapy in the metastatic setting
- No disease recurrence ≤6 mo after completion of adjuvant/neoadjuvant chemotherapy

Stratification Factors

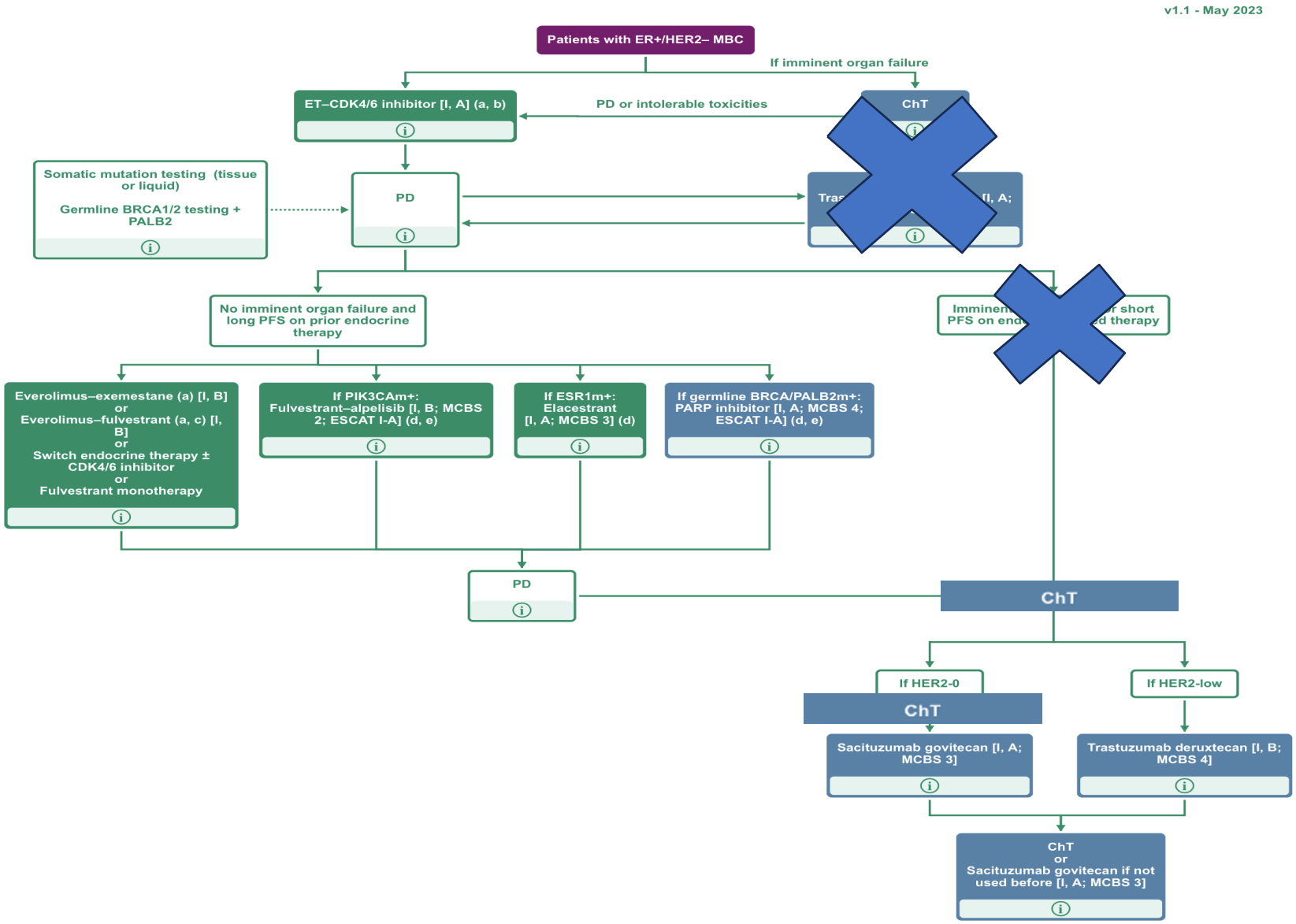
- PD-L1 (CPS <1 vs 1–9 vs ≥10)
- TROP2 expression per IHC (low + medium vs high)
- Geographic region (Western Europe vs North America vs Rest of World)

R (3:3:2)
N ~ 1200

- Sac-TMT 4 mg/kg IV Q2W
- Sac-TMT 4 mg/kg IV Q2W + Pembrolizumab 400 mg IV Q6W
- TPC (paclitaxel, nab-paclitaxel, capecitabine, or liposomal doxorubicin)

Tolaney SABCS 2024.

Algoritmo actual


v1.1 - May 2023
Patients with ER+/HER2– MBC
If imminent organ failure
ET–CDK4/6 inhibitor [I, A] (a, b)
PD or intolerable toxicities
ChT
Somatic mutation testing (tissue or liquid)
Germline BRCA1/2 testing + PALB2
PD
No imminent organ failure and long PFS on prior endocrine therapy
Everolimus–exemestane (a) [I, B]
or
Everolimus–fulvestrant (a, c) [I, B]
or
Switch endocrine therapy ± CDK4/6 inhibitor
or
Fulvestrant monotherapy
If PIK3CAm+: Fulvestrant–alpelisib [I, B; MCBS 2; ESCAT I-A] (d, e)
If ESR1m+: Elacestrant [I, A; MCBS 3] (d)
If germline BRCA/PALB2m+: PARP inhibitor [I, A; MCBS 4; ESCAT I-A] (d, e)
PD
ChT
If HER2-0
ChT
Sacituzumab govitecan [I, A; MCBS 3]
If HER2-low
Trastuzumab deruxtecan [I, B; MCBS 4]
ChT
or
Sacituzumab govitecan if not used before [I, A; MCBS 3]

Conclusiones

- TROP2 se convierte en una diana terapéutica en cáncer de mama Luminal avanzado.

- 3 antiTROP2 en desarrollo.

- Indicación y financiación de tratamiento con SACITUZUMAB GOVITECAN en cáncer de mama metastásico Luminal HER2- en base a los resultados del estudio TROPICS-02

- Nuevas alternativas por llegar

GRacias!

II JORNADA TRASLACIONAL DE ONCOLOGÍA DE PRECISIÓN: A TRAVÉS DE LAS VÍAS DE SEÑALIZACIÓN

SEVILLA, 6 Y 7 DE FEBRERO DE 2025